REMARKS

Prior to entry of this amendment, claims 1 and 4-37 were pending and claims 1, 4-10, 14-18, and 27-37 were under consideration. With this amendment, claims 1 and 9 are canceled, and claims 4, 5, 14, and 29-32 are amended to better define the invention. Support for those amendments can be found throughout the specification and in the claims as originally filed. No new subject matter has been added.

Claim Interpretation

The Action alleged that

> [t]he terms referring to 'target nucleic acids comprising essentially of all or part of the sequence of a gene or a genomic sequence...comprise at least one CpG dinucleotide sequence' (see claim 1) are being given the broadest reasonable interpretation in light of the specification. While Applicant may intend for the at least one CpG dinucleotide to be detected in the context of the sequence as claimed, as currently recited, the claim reads on any CpG dinucleotide with any degree of complementarity to the claimed genes or specific sequences.

Claim 1 has been cancelled. Solely to expedite prosecution and without acquiescing to the rejection, claim 5 has been amended to recite a method comprising a reagent "wherein the at least one reagent comprises a single stranded nucleic acid molecule or peptide nucleic acid at least 9 nucleotides in length that hybridizes under stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 130, 131, 248, 249 and complements thereof." Solely to expedite prosecution and without acquiescing to the rejection, claim 14 has been amended to recite a method comprising primers "wherein each primer comprises a single stranded nucleic acid molecule at least 9 nucleotides in length that hybridizes under stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 130, 131, 248, 249 and complements thereof."

Applicants assert that amended claims 5 and 14 recite reagents or primers comprising a single stranded nucleic acid molecule at least 9 nucleotides in length that hybridizes under

stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 130, 131, 248, 249 and complements thereof.

Rejections under 35 USC § 112

Claims 1, 4-10, 14-18 and 28-32 are rejected under 35 USC § 112 for allegedly failing to comply with the written description requirement. Applicants respectfully traverse this rejection.

The Office Action alleged that "the claims encompass a genus of nucleic acids that comprise sequences capable of binding to SEQ ID NO: 36, 130, and 131." The Action further alleged that "[t]here are no limitations or instructions provided regarding the minimum number of complementary nucleic acids...." The Action further alleged that "not only are there no structural limitations or requirements which provide guidance on the identification of nucleic acids related to SEQ ID NO: 36, 130 and 131, but there are no functional limitations in the claim either." The Action further alleged that "only four species are disclosed, SEQ ID NO: 36, 130 and 131. These species represent a specific nucleic acid sequence and are not representative of the entire genus." The Action further alleged that there is no structure which the specification demonstrates is necessarily correlated with the primer or probe functions of the nucleic acid of SEQ ID NO: 36, 130 and 131.

The MPEP states that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by a) actual reduction to practice or b) relevant, identifying characteristics. Relevant identifying characteristics in turn include: 1) structure or other physical and/or chemical properties; 2) functional characteristics coupled with a known or disclosed correlation between function and structure; or 3) a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. MPEP at 2163. The MPEP further states that in the case of biomolecules, examples of identifying characteristics include a sequence, structure, binding affinity, binding specificity, molecular weight, and length. Id.

Claims 1, 5, and 14 are independent claims. Claim 1 has been cancelled. Amended claim 5 recites a method comprising a reagent "wherein the at least one reagent comprises a single stranded nucleic acid molecule or peptide nucleic acid at least 9 nucleotides in length that hybridizes under stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 130, 131, 248, 249 and complements thereof." Amended claim 14 recites a method comprising primers "wherein each primer a single stranded nucleic acid molecule at least 9 nucleotides in length that hybridizes under stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 130, 131, 248, 249 and complements thereof."

Applicants assert that amended claims 5 and 14 recite sufficient structural characteristics to meet the written description requirement for the claimed genera. Each of those claims recites the structure, binding affinity, binding specificity, and length – thus four of the six examples of such characteristics provided in the MPEP -- of a claimed reagent or primer. Specifically, each claim recites that the claimed reagent or primer is a single stranded nucleic acid (or peptide nucleic acid in the case of claim 5) (structure), at least 9 nucleotides in length (length), hybridizes under stringent conditions (binding affinity), and hybridizes to SEQ ID NO: 130, 131, 248, 249 and complements thereof (binding specificity). Further structural elements of nucleic acids and peptide nucleic acids, for example their chemical composition, were known in the art and were thus not required to be disclosed in the specification.

Additionally, the specification discloses a correlation between a function and a structure of the claimed reagents and primers. Specifically, claims 5 and 14 recite methods for detecting and/or distinguishing between or among prostate cell proliferative disorders. The specification discloses that after treating DNA with certain compounds, for example bisulfite, "cytosine is converted to uracil which corresponds to thymine in its base pairing behavior....however, 5-methyl-cytosine remains unmodified...." Specification at page 17, lines 9-18. Thus, the specification discloses a correlation between a function of the disclosed reagents or primers, i.e. detecting and/or distinguishing between or among prostate cell proliferative disorders, and the

structure of those reagents or primers, i.e. their sequence at the position corresponding to a target CpG in the treated genomic DNA.

Still further, although a specification can meet the written description requirement for a genus by disclosing relevant structural characteristics and/or a correlation between structure and function, and thus is not required to disclose any species, the specification nevertheless discloses an example of a primer pair of claim 14 at Table 15, page 124.

Applicants assert that between the disclosed structural characteristics, disclosed correlation between function and structure, and disclosed species, the specification discloses sufficient detail to prove that they were in possession of the claimed genera of claims 5 and 14. Further, claims 4, 6-8, 10, 15-18, and 28-32 depend from claim 5 or 14 and thus also meet the written description requirement. Claims 1 and 9 have been canceled. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Rejections under 35 USC § 102

Claims 1, 4-10, 14-18 and 27-32 are rejected under 35 USC 102(a) or (e) as allegedly being anticipated by Distler et al. (WO02/103042). Applicants respectfully traverse this rejection.

With regard to claim 14, the Office Action alleges that Distler teaches a method "where prostate cancer is differentiated and where any of the CpG dinucleotides read on the claim as currently broadly recited – see claim interpretation above)."

In order to anticipate a claim, a reference must teach each and every element of that claim. See, e.g, MPEP at 2131.

Applicants assert that Distler et al. fails to teach each and every element of amended claim 5 (from which amended claim 4 depends) or amended claim 14. For example, Distler et al. fails to teach a method comprising a reagent "wherein the at least ne reagent comprises a single

stranded nucleic acid molecule or peptide nucleic acid at least 9 nucleotides in length that hybridizes under stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 130, 131, 248, 249 and complements thereof." Distler et al. also fails to teach a method comprising primers "wherein each primer comprises a single stranded nucleic acid molecule at least 9 nucleotides in length that hybridizes under stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 130, 131, 248, 249 and complements thereof," as recited in amended claim 14. Distler et al. discusses genes that are subjected to methylation analysis in order to distinguish between benign prostate hyperplasia and prostate carcinoma. However, histone H4, which corresponds to the sequences recited in amended claims 5 and 14, is not one of those genes. On the contrary, there is no teaching or suggestion of histone H4 or SEQ ID NOS: 130, 131, 248, 249 and complements thereof in Distler et al. Thus, Distler does not anticipate claim 5 or 14, or any of claims 4, 15-18, and 27-32, which depend from claim 5 or 14. Claim 1 has been cancelled. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

IV. Claim Rejections under 35 USC § 103

Claims 5-10 and 29-37 are rejected under 35 USC § 103(a) as allegedly being unpatentable over Distler et al. (WO92/103042) in view of Wang et al. (US Patent H002220) and Buck et al. (Biotechniques 1999, 27, p. 528-536). Applicants respectfully traverse the rejection.

The Office Action alleged that with regard to claim 5, Distler et al teaches a method where prostate cancer is differentiated based on the analysis of methylation status of CpG dinucleotides in multiple genes using a set of primers as recited in Table 1. The Action further stated "Distler does not specifically teach at least 16 contiguous nucleotides of a sequence according to SEQ ID NO: 36."

The Action alleged, however, that "Wang teaches sequence hybridizes to at least 16 contiguous nucleotides of s sequence taken from the group consisting of SEQ ID NO: 36 (see alignment below, where SEQ ID NO: 793719 of Wang teaches complementarity to SEQ ID NO:

36)." The Action further alleged that Wang et al. teaches "sequence comprising contiguous sequence at least 9 nucleotides in length selected from the group consisting of SEQ ID NO: 130, 131 and contiguous regions thereof corresponding to the target sequence or a complement thereof (see alignment below, where SEQ ID NO: 793719 of Wang comprises at least 9 contiguous nucleotides of SEQ ID NO: 130 and SEQ ID NO: 131).

The Action further alleged that "Buck provides evidence of the equivalence of primers."

Under 35 U.S.C. §103, as that statute was interpreted by the Supreme Court in *KSR International Co. v. Teleflex Inc.*, 82 USPQ 2d 1385 (2007), a claim is invalid if: a) prior art documents disclose each element of the claim; b) the results of combining those elements were predictable to one skilled in the art; and c) and one skilled in the art would have been motivated to combine those elements. MPEP at 2143.

Applicants assert that the Examiner has failed to establish a prima facie case of obviousness for claim 5 or claim 14 (from which claims 29-37 depend). As discussed above, Distler et al. fails to teach the reagents or primers recited in amended claims 5 or 14. Further, Wang et al. fails to remedy that deficiency. Wang et al. discusses SNP probes. Wang et al. also discloses almost one million SEQ ID NOS. One of those SEQ ID NOS. is a 558 nucleotide sequence that corresponds to SEQ ID NO: 36, which corresponds to the histone H4 gene. However, Wang does not teach or suggest reagents or primers that hybridize under stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 130, 131, 248, 249 and complements thereof, which correspond to the sequences of bisulfite-treated methylated or unmethylated histone H4 sequences. There is nothing in the disclosure of a sequence corresponding to histone H4 in a document that discusses SNPs and and discloses close to 1 million sequences that teaches or suggests reagents or primers to bisulfite-treated methylated or unmethylated sequences in the histone H4 gene.

Further, claims 5 and 14 recite methods for detecting and/or distinguishing between or among prostate cell proliferative disorders in a subject, wherein the methods comprise, in

addition to the recited reagents and primers, steps that comprise determining the methylation state of at least one CpG dinucleotide. Wang certainly does not teach or suggest such steps.

Further, Buck et al. fails to remedy the deficiencies of Distler et al. and Buck et al. Buck et al. discusses does not teach or suggest the recited reagents or primers, much less methods comprising those reagents or primers.

Therefore, because none of Distler et al., Wang et al., or Buck et al., alone or in combination, discloses each and every element of claim 5 or claim 14, the Examiner has failed to establish a prima facie case of obviousness for those claims, or for claims 6-8 and 29-37, which depend from claim 5 or claim 14. Claim 9 has been canceled. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

CONCLUSION

In view of the foregoing amendments and the remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this case.

Please charge Deposit Account No. 07-1896 in the amount of $1,100 to cover the Three-Months Extension of Time fee ($635.00) and the Request for Continued Examination fee ($465.00). No additional fee is believed to be due in connection with this submission. However, the Commissioner is hereby authorized to charge any other fees associated with the filing submitted herewith, or credit any overpayments to Deposit Account No. 07-1896 referencing the above-identified attorney docket number.

Respectfully submitted,

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